Exhibit A

1: Pancreas 1989;4(3):282-8

Peptide YY: intrapancreatic localization and effects on insulin and glucagon secretion in the mouse.

Bottcher G, Ahren B, Lundquist I, Sundler F.

Department of Medical Cell Research, Lund University, Sweden.

We studied the intrapancreatic localization of peptide YY (PYY) and the effects of PYY on insulin and glucagon secretion in the mouse. Immunofluorescence staining of mouse pancreatic tissue showed that PYY occurred within islet cells. These cells were located preferentially at the periphery of the islets. Sequential and simultaneous double immunostaining revealed that most PYY cells also displayed glucagon immunoreactivity; some PYY cells contained immunoreactive pancreatic polypeptide (PP). At the electromicroscopic level, PYY immunoreactivity was demonstrated within the secretory granules of both glucagon cells and of a small granular cell type, which showed structural similarities to PP cells. In in vivo experiments, PYY at dose levels between 0.53 and 8.5 nmol/kg had no influence on basal plasma levels of insulin, glucagon, or glucose. In contrast, insulin secretion stimulated by glucose or the cholinergic agonist carbachol was inhibited by PYY (by 33 and 26%, respectively, at 4.25 nmol/kg). Similarly, carbachol-induced glucagon secretion was inhibited by PYY (by 47% at 4.25 nmol/kg). We conclude that PYY occurs in islet cells of the mouse pancreas, most of which are glucagon cells, and that PYY inhibits stimulated insulin and glucagon secretion in vivo in the mouse.

PMID: 2660131 [PubMed - indexed for MEDLINE]

1: Pancreas 1992;7(5):595-600

Related Articles, Books

Evidence for a direct inhibitory effect of PYY on insulin secretion in rats.

Bertrand G, Gross R, Roye M, Ahren B, Ribes G.

Faculte de Medecine, Laboratoire de Pharmacologie et Pharmacodynamie, CNRS URA 599, Montpellier, France.

Peptide YY (PYY) has been shown to inhibit stimulated insulin secretion under in vivo conditions in the mouse, the rat, and the dog. In the present study, we investigated the effects of PYY on insulin secretion from the isolated perfused rat pancreas and isolated rat islets. In isolated pancreas perfused in presence of 8.3 mM glucose, PYY at 10(-10) and 10(-9) M, but not at 10(-8) M, inhibited insulin secretion. In the presence of 5.5 mM glucose, PYY (10(-9) M) did not modify basal insulin release but reduced the biphasic insulin response to arginine (10 mM). PYY also markedly reduced the pancreatic vascular flow rate; this effect was observed at all three concentrations tested in a dose-dependent manner. In isolated islets, glucose (15 mM)-stimulated insulin secretion was inhibited by PYY at 10(-7) M. We conclude that in the perfused rat pancreas, PYY inhibits insulin secretion and induces vasoconstriction without a causal relationship. In addition, our results on isolated islets suggest that the inhibitory action of PYY on insulin secretion is exerted through a direct islet action.

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